A peptide-based cell-cell communication mechanism in *Streptococcus agalactiae*

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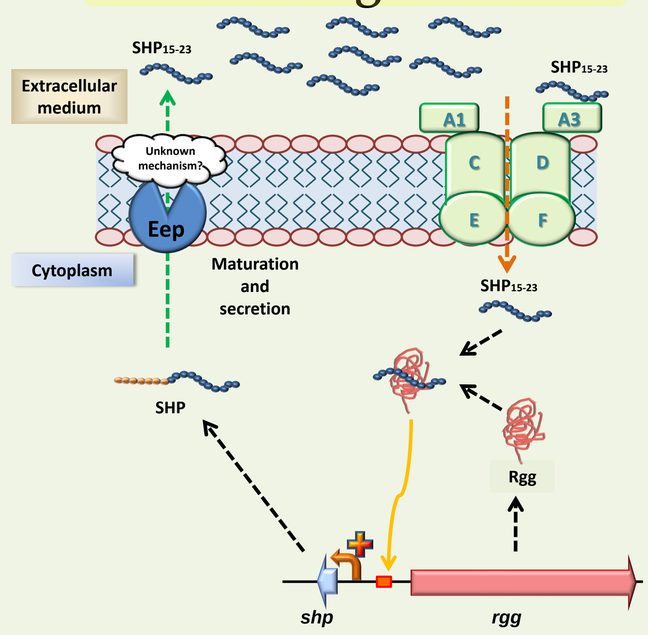
Background

Quorum-sensing (QS) is a cell-cell communication mechanism in bacteria that controls gene expression via secreted signaling molecules. Recently, a new QS mechanism was described in streptococcaceae in which a small hydrophobic peptide (SHP) is produced, secreted, matured and re-imported into the cell to interact with a Rgg-like transcriptional regulator. This interaction controls the activity of Rgg and positively regulates the expression of its targets, among which is *shp* itself[1].



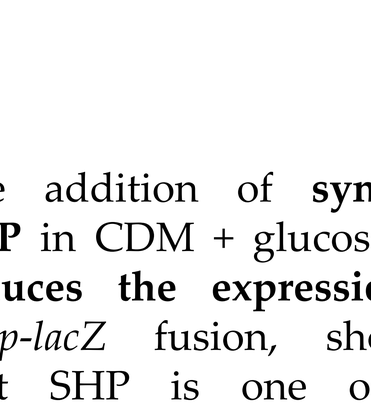
Streptococcus agalactiae or Group B Streptococci (GBS) is a Gram positive bacterium that causes devastating infections mainly in newborns. The Rgg-like RovS transcriptional regulator controls the expression of several GBS virulence factors[2]. However, SHP was not identified in this previous work and experiments were done in growth conditions that probably inhibited rather than stimulated RovS activity. Consequently, we believe that RovS relevance in the pathogeny of GBS has been underestimated.

Observations

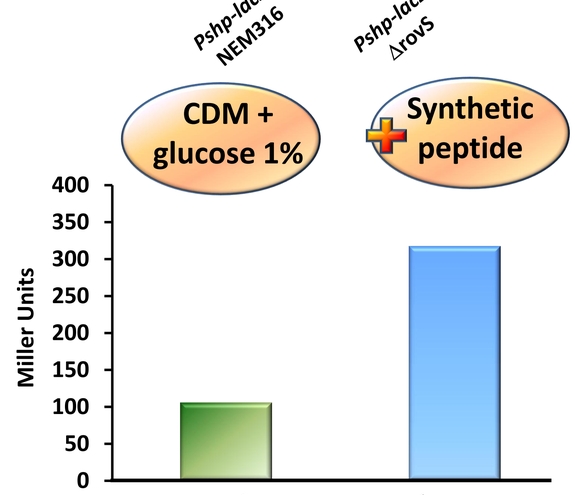
1.Is SHP/RovS QS mechanism active in GBS?

A transcriptional fusion between promoter region of *shp* and *lac*Z in strain NEM316 of GBS, was used to identify good growth conditions for RovS targets expression.

P*shp-LacZ* transcriptional fusion



Chemically defined medium (CDM): **free of peptides!!**



The construction of Δ*rovS* deletion mutant in strain NEM316 showed that P*shp-lacZ* fusion is **not expressed** in this genetic environment, demonstrating that RovS controls positively *shp* expression.

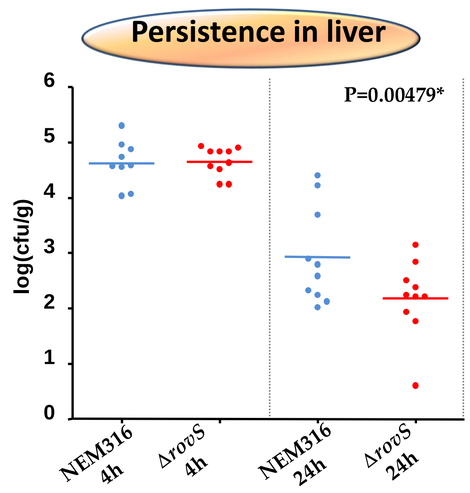
The addition of **synthetic SHP** in CDM + glucose 1 % **induces the expression** of P*shp-lacZ* fusion, showing that SHP is one of the components of this QS mechanism.

SHP/RovS QS mechanism is active in strain NEM316 of GBS

2. Is RovS involved in virulence?

Virulence results on 6 week-old mice showed that the *rovS* mutant, injected via intravenous route, displays lower ability to persist in liver after 24 h post-injection than the wild-type strain.

Persistence in liver

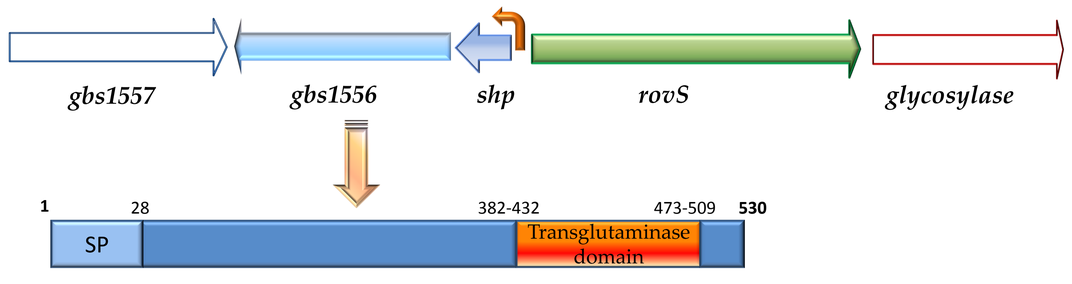


SHP/RovS QS system is involved in the persistence of strain NEM316 of GBS

3. What are targets of RovS?

The secretomes of strain NEM316 and Δ*rovS* mutant were compared using a label free proteomic approach to identify targets regulated by the SHP/RovS QS system.

Identified new target, *gbs1556*, encodes a secreted protein with unknown function that presents a transglutaminase domain only presents in *Streptococcus pyogenes*, *Streptococcus dysgalactiae* and *Streptococcus ictaluris*, besides all sequenced GBS strains.



SHP/RovS QS system controls the expression of GBS1556 in NEM316 GBS strain

References

1.**Fleuchot, B.,** et al., *Rgg proteins associated with internalized small hydrophobic peptides: a new quorum-sensing mechanism in streptococci.* Mol. Microbiol., 2011. **80**: 1102-1119.
2.**Samen, U.M.,** et al, *The transcriptional regulator RovS controls the attachment of Streptococcus agalactiae to human epithelial cells and the expression of virulence genes.* Infect. Immun., 2006. **74**: 5625-5635.

Conclusions

1. *SHP/RovS sQS ystem is active in GBS.*
2. *SHP/RovS QS mechanism seems to be involved in the persistence of GBS in vivo.*
3. *shp and gbs1556 are target genes of this QS mechanism.*